

## Case reports

### Congenital insensitivity to pain

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**Keywords:** analgesia; congenital

Congenital insensitivity to pain is a rare inherited disorder which presents with unusual injuries due to repetitive self-inflicted damage. The diagnosis is often delayed and management a problem.

#### Case report

The affected girl was born in the United Kingdom to Pakistani parents who are first cousins. She was referred at 13 months of age with recurrent severe ulceration of the lips and tongue. When bullous-like lesions appeared on the fingers and toes, epidermolysis bullosa was diagnosed.

At the age of two she developed a swollen left foot. Radiological examination showed lysis of the first metatarsal with callus formation. Similar destructive changes were evident in the left hip and shoulder. Skin biopsy was normal and open biopsy of the first metatarsal excluded infective or malignant cause. Postoperatively, she mobilized immediately resulting in destruction of the plaster on her foot, and it was apparent that she did not feel pain. Shortly afterwards she sustained fractures to both arms and frequent cutaneous injuries (Figure 1).

Sensory examination, including light torch, proprioception, vibration and temperature sensation were intact. Deep tendon and corneal reflexes were present. Pinprick was recognized over the whole of her body, but she did not feel discomfort. There were no autonomic disturbances - she sweated normally and produced tears. Motor and sensory nerve conduction velocity studies and intellectual assessment were normal.

Family studies revealed a second cousin with congenital insensitivity to pain and two further similarly affected children in Pakistan who have not been formally evaluated. These children are all products of first cousin marriages within the same extended family (Figure 2). Autosomal recessive inheritance has been suggested.

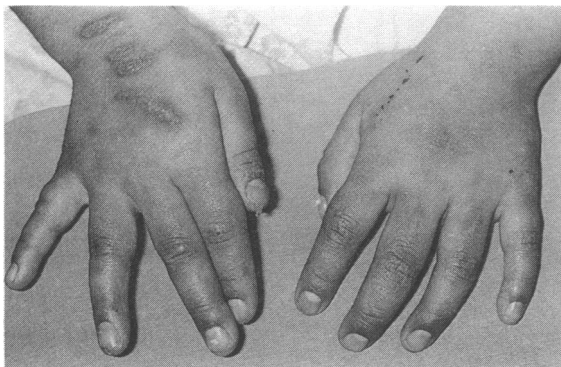
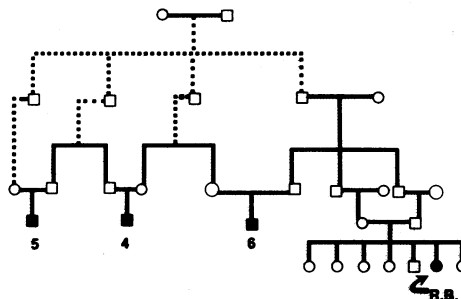


Figure 1. Unexplained burns and abrasions to hands

#### FAMILY HISTORY



**INHERITANCE:** AUTOSOMAL RECESSIVE

Figure 2. Family tree: RB ● is index case, ■ other affected children (ages in years)

#### Discussion

Since the first description of a carnival performer who earned his living as 'The Human Pincushion'<sup>1</sup> there have been over 40 reported cases of congenital insensitivity to pain that fulfil the criteria of Thrush<sup>2</sup> - pain sensation is absent from birth, the entire body is affected, all other sensory modalities are intact and the deep tendon reflexes are preserved. (These findings exclude other conditions with reduced sensitivity to pain; the congenital sensory neuropathies.)

Self-mutilation tends to start at the time of initial tooth eruption with biting of the tongue and digits. Charcot's joints result from repeated minor trauma and major trauma. Our patient's first cousin presented with an unexplained fracture, bruising and burns which was initially mistaken for non-accidental injury<sup>3</sup>.

The cause remains unknown. Morphometric studies of the sural nerve have demonstrated a peripheral neuropathy, with selective reduction of A delta fibres<sup>4</sup>. This would not explain complete analgesia. Overproduction of endogenous neuropeptides is a factor in some patients. Experimentally, naloxone, a specific opiate antagonist has been found to reverse analgesia for short periods or modify the physiological response to a painful stimulus<sup>5</sup>.

Since protecting these children poses a significant management problem, with unrecognized intra-abdominal pathology and destructive neuropathic arthropathy of lower limbs and spine as continuing hazards, we attempted to evaluate the therapeutic value of naloxone in our 5-year-old patient, by observing the reflex withdrawal response following peripheral nerve stimulation. Repetitive stimuli to a maximum voltage of 250 volts produced neither reflex withdrawal nor any complaint from the patient. Following the administration of naloxone 0.4 mg intravenously the child complained of discomfort but there was no measurable difference in reflex response to the painful stimuli. Since the results were inconclusive, a trial of naltrexone, a long lasting orally active opiate antagonist, was employed, which also failed to reverse analgesia in a dose of 25 mg daily. Many questions about the mechanism of congenital insensitivity to pain remain unanswered.

#### References

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Case presented  
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## Cutaneous aspects of Refsum's disease

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**Keywords:** Refsum's disease; hereditary ataxia polyneuritis; phytanic acid; ichthyosis; high pressure thin layer chromatography

We report a patient with severe Refsum's disease and describe her cutaneous findings. She had a good response to reduction of serum phytanic acid and we emphasize the importance of careful dietary management of this condition.

### Case report

A 24-year-old woman presented in June 1989 with a one month history of weakness, dizziness and unsteadiness. There was associated numbness in both feet, ringing in the ears, headache and a 3 week history of difficulty writing and typing. She gave a history of intermittent deafness over the preceding 5 years increasing over the last few months. One year prior to admission she had returned to live with her mother, found the diet unpalatable and ate less with consequent rapid weight loss.

Examination revealed moderately severe truncal and four limb cerebellar ataxia rendering her unable to walk, a peripheral sensory and motor neuropathy, sensory nerve deafness and fundal changes compatible with retinitis pigmentosa. She was strikingly thin with ichthyotic skin over her lower back, waist, upper arms and thighs.

A skin biopsy from the waist showed a hyperkeratotic epidermis. Many of the basal cells were finely vacuolated.

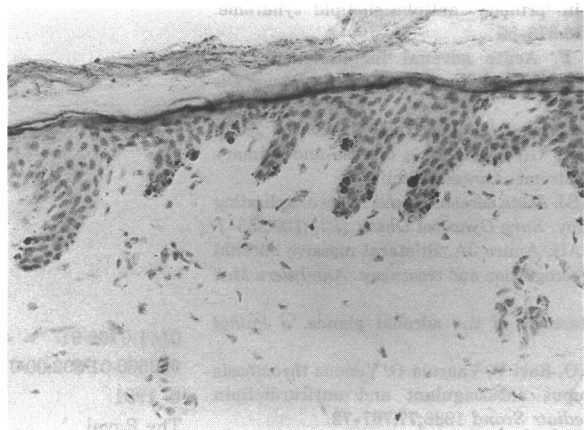


Figure 1. Epidermal hyperkeratosis and fat globules within the vacuolated basal cells (Oil-Red-O×8.5)

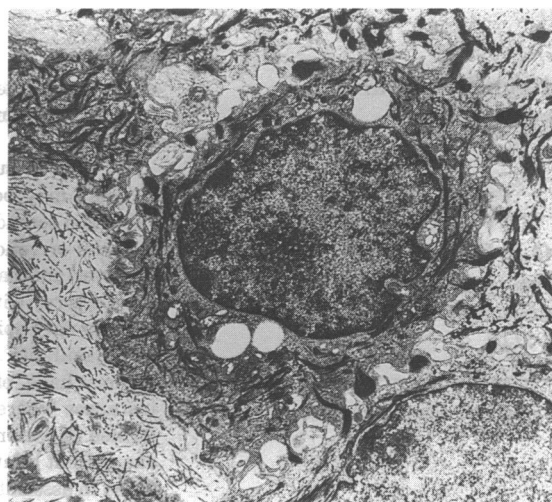


Figure 2. Electron micrograph of epidermal basal cell showing lipid laden droplet

Oil-red O stain demonstrated numerous fat globules within the basal cell layer and other keratinocytes (Figure 1). Histology from uninvolved skin showed similar though less marked changes. Small lipid droplets were seen on electron microscopy within basal keratinocytes (Figure 2).

Her initial serum phytanic acid level was greater than 2000 µmol/l (normal 20-30 µmol/l). HPTLC analysis was performed on her skin scale lipid extracts and showed free fatty acid 9.7% of lipid extract. Fatty acid analysis of scale lipid phospholipid and free fatty acids showed an excess of short chain and a reduction in long chain fatty acids. Plasma phospholipid and red cell membrane phospholipid had similar reduction in the longer chain fatty acids, linoleic acid and oleic acid. An aberrant serum peak of a complex fatty acid thought to be phytanic acid comprised 3% all serum fatty acids.

A low phytanic acid diet and four plasma exchanges resulted in large decrease in serum phytanic acid<sup>1,4</sup>. Weight gain was difficult on the diet. Nasogastric feeds and close supervision by the dieticians were required before the patient put on weight. Her peripheral neuropathy and ability to walk have improved. Her ichthyosis disappeared gradually. There was modest improvement in her hearing.

### Discussion

This patient had an acute presentation of Refsum's disease (hereditary ataxia polyneuritis, HAP). The primary biochemical defect is an inability to convert dietary phytanic acid (a C20 fatty acid with methyl side groups) to alpha-hydroxyphytanic acid. This leads to an accumulation of phytanic acid most of which is deposited in adipose tissue. The rapid development of widespread neuropathy and rash which precipitated referral was preceded by a period of low calorie intake and was due to mobilization of phytanic acid from adipose tissue<sup>1</sup>. Phytanic acid can be excreted through the skin and this route must be inundated with very high serum concentrations of phytanic acid. The mechanism of the ichthyosis in HAP is unknown but there is a high epidermal labelling index<sup>2</sup>. The accumulation of phytanic acid in the epidermis appears to cause an imbalance in long

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